REMARKS

Claims 1, 8, 10-13, 18, 22, 31 and 33-39 are pending the application; all are subject to further restriction and/or election. By this Amendment Claims 1, 8, 10-13 and 22 have been canceled, Claims 18 and 31 have been amended, and new claims 40-51 have been added. These amendments and new claims add no new matter to the application.

The Examiner has identified three further species: VIII (Claims 1, 8, 31 and 33-38); IX (Claims 10--13, 22, 31 and 33-38); and X (Claims 18, 31, and 33-38). Applicant herewith elects species X (Claims 18, 31, and 33-38) for examination on the merits. Applicant herewith also elects Claim 39 and new Claims 40-51 for examination on the merits. Applicant inadvertently left off then new claim 39 from inclusion in the previous election, but believes the claim is drawn to the elected invention. New claims 40-51 are variations on elected claims and are believed includable in the same election.

Applicant believes it has responded fully to all of the concerns expressed by the Examiner and respectfully requests that the claims be amended as indicated, and that early favorable action be taken on all claims pending in the application. If the Examiner has any further concerns, Applicant requests a call to Patrick Dwyer at (206) 343-7074.

Respectfully submitted,

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Claims Listing

1-17 (Cancelled)

18. A method for isolating amyloid inhibitory ~~water-soluble~~ components from *Uncaria tomentosa* ~~that possess amyloid inhibitory activity~~, the method comprising the steps:

a) adding 4000ml of methanol to 1 kg of *Uncaria tomentosa* and mixing

b) centrifuging the mixture at X2,500g using a centrifuge for 30 minutes and collecting the supernatant;

c) extracting the insoluble material about 3 more times as steps a and b above;

d) combining the supernatants and evaporating to dryness (or until about 500 ml volume is reached) using a rotary evaporator at 50°C,

e) taking the powdered extract (or about 500ml volume), washing 4 times with 300ml of petroleum ether, and discarding the ether layer,

f) evaporating the methanol to dryness using a rotary evaporator at 50°C;

g) extracting the solid material 5 times with 150ml of distilled water, followed by centrifugation at 2,500Xg for 30 minutes each time;

h) combining the supernatants and then lyophilizing using a freeze-dryer;

i) dissolving the resulting lyophilized extract into about 500 ml of distilled water, and applying 50-100ml portions to a 400 ml LH-20 column equilibrated with distilled water.

j) eluting the LH-20 column with 1,100ml of distilled water (~3 column volumes) and discarding the amber/yellow, non-active fractions;

k) eluting the LH-20 column with 1,100ml of 100% methanol (~3 column volumes) and collecting a set of active fractions and evaporating to dryness using a rotary evaporator at 50°C;

l) dissolving the fractions of step k in water (80mg/ml) and applying 5 ml at a time to a 10gm disposable C18 SPE column equilibrated in solvent A (solvent A is 95% water/5% acetonitrile/0.1% TFA);

m) washing the column with 3 volumes of solvent A and discarding the eluate;

n) eluting the column with 3 volumes of solvent A containing 12.5% solvent B (solvent B is 95% acetonitrile/5% water/0.1% TFA) and lyophilizing the eluate;

o) taking 50mg of the lyophilized eluate of step n and injecting multiple times into a Hewlett-Packard 1100 Series HPLC instrument with diode array detector, fitted with a 2.2cm X 25 cm Vydac 218TP1022 C18 reverse-phase column maintained at 25°C and at a flow rate of 5 ml/min;

p) eluting the sample with the following solvent profile, 10% B for 0 to 20 minutes, 10-100 % B gradient for minutes 20 to 30, and 100-10% B gradient for minutes 30-31, where B is 95% acetonitrile/5% water/0.1% TFA;

q) and separating and collecting ~~the~~ at least one fractions component~~into~~ selected from the group of fraction ~~11 major~~ components defined as fraction G (~13-14 minutes), fraction F (~15-16 minutes), fraction H (~17-20 minutes), fraction I (~21 minutes), fraction J (~22 - 23 minutes), fraction K1 (~24 minutes), fraction K2 (~25 minutes), fraction L (~26-27 minutes), fraction M (~27-28 minutes), and fraction N (~28-29 minutes).

19-30 (Cancelled)

31. A pharmaceutical agent comprising a therapeutically effective amount of a material made according to the process of claim~~s 1, 8, 10-13,~~ 18 ~~or 22~~, the therapeutic amount of the material selected for efficacy in treating an amyloid disease or a disease related to alpha-synuclein in a patient.

32. (Cancelled)

33. The pharmaceutical agent of claim 31 wherein the therapeutically effective amount of a material comprises a dosage in the range of from about 10 to 1,000 mg/kg of body weight of the patient.

34. The pharmaceutical agent of claim 33 wherein the therapeutically effective amount of a material comprises a dosage in the range of from about 10 to 100 mg/kg of body weight of the patient.

35. The pharmacological agent of claim 33 wherein said amyloid disease for treatment is selected from the group of amyloid diseases associated with Alzheimer's disease, Down's syndrome, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, the amyloidosis associated with type II diabetes, the amyloidosis associated with chronic inflammation, various forms of malignancy and Familial Mediterranean Fever, the amyloidosis associated with multiple myeloma and other B-cell dyscrasias, the amyloidosis associated with the prion diseases including Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, kuru and animal scrapie, the amyloidosis associated with long-term hemodialysis and carpal tunnel syndrome, and the amyloidosis associated with endocrine tumors such as medullary carcinoma of the thyroid, and the alpha-synuclein associated disease is selected from Parkinson's disease and Lewy body disease.

36. The pharmacological agent of claim 35 wherein said amyloid disease for treatment is Alzheimer's disease.

37. The pharmacological agent of claim 33 further comprising a pharmaceutically acceptable carrier, diluent, or excipient.

38. The pharmacological agent of claim 33 wherein the therapeutically effective amount of the material has an amyloid inhibitory activity or efficacy greater than 50%.

39. The pharmacological agent of claim 35 wherein the disease related to alpha-synuclein is Parkinson's disease.

40. (New) A method for isolating amyloid inhibitory components from *Uncaria tomentosa* plant matter, the method comprising the steps:

a) preparing a polar solvent extract of the plant matter, where the polar solvent extraction is selected from one of the extraction methods from the group of extraction methods consisting of extraction with water, extraction with a water solution of a polar alcohol, extraction with a water solution of acetonitrile, and extraction with a water solution of another polar organic solvent selected from the group of polar organic solvents consisting of triethanolamine, acetone, and the like;

b) running the extract through a first column that comprises hydroxy group containing resin, or resin having hydrophobic characteristics but without any hydroxy groups, or a mixture of both;

c) eluting the first column with distilled water, followed by eluting with not more than 2-4 column bed volume washings with a dilute polar alcohol/water solution having an alcohol/water ratio not greater than 50/50, and discarding any eluate;

d) eluting the first column with one or more column bed volume washings of a polar alcohol/water solution having an alcohol/water ratio between 50/50 and substantially pure alcohol, and collecting and drying the eluted volumes to a dried material;

e) applying an aqueous solution of the dried material to a second column comprising a hydrophobic resin, the second column having been preparatorily equilibrated in a solvent A comprising about 95% water/5% acetonitrile, and then eluting the second column with more solvent A and discarding the eluate;

f) eluting the second column with a mixture of solvent A containing 10-15% of a solvent B comprising about 95% acetonitrile/5% water and collecting and drying the eluted volumes to a dried material;

g) making one or more injections of a solution of the dried material in a solvent selected from the group of solvents consisting of water, water/dilute alcohol and solvent comprising solvent A and no more than 10% solvent B, into an HPLC instrument having a diode array uv/vis detector with a graphic display, the HPLC instrument further comprising a reverse-phase column;

h) eluting the material through the HPLC column using a solvent gradient profile as follows: 10% solvent B for about the first 20 minutes from start of elution, 10 to 100% solvent B gradient for about minutes 20 to 30 from start of elution, and 100 to 10% solvent B gradient for about minutes 30 to 32 from start of elution, while observing graphic display peaks over time on the uv/vis detector during the elution gradient; and

i) separating the eluate and collecting at least one fraction component at a selected elution time, the fraction selected from the group of fraction components defined with elution times as fraction G (~13-14 minutes), fraction F (~15-16 minutes), fraction H (~17-20 minutes), fraction I (~21 minutes), fraction J (~22 - 23 minutes), fraction K1 (~24 minutes), fraction K2 (~25 minutes), fraction L (~26-27 minutes), fraction M (~27-28 minutes), and fraction N (~28-29 minutes), the elution times corresponding to times associated with the graphic display peaks.

41. (New) The method of Claim 40 wherein the polar solvent extract of step a is an extraction in methanol, the elution of step f is an elution with sovent A containing about 12.5% solvent B, and at least one of the fractions collected in step i is fraction H (~17-20 minutes).

42. (New) A pharmaceutical agent comprising a therapeutically effective amount of a material made according to the process of claims 40, the therapeutic amount of the material selected for efficacy in treating an amyloid disease or a disease related to alpha-synuclein in a patient.

43. (New) The pharmaceutical agent of claim 42 wherein the therapeutically effective amount of a material comprises a dosage in the range of from about 10 to 1,000 mg/kg of body weight of the patient.

44. (New) The pharmaceutical agent of claim 43 wherein the therapeutically effective amount of a material comprises a dosage in the range of from about 10 to 100 mg/kg of body weight of the patient.

45. (New) The pharmacological agent of claim 43 wherein said amyloid disease for treatment is selected from the group of amyloid diseases associated with Alzheimer's disease, Down's syndrome, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, the amyloidosis associated with type II diabetes, the amyloidosis associated with chronic inflammation, various forms of malignancy and Familial Mediterranean Fever, the amyloidosis associated with multiple myeloma and other B-cell dyscrasias, the amyloidosis associated with the prion diseases including Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, kuru and animal scrapie, the amyloidosis associated with long-term hemodialysis and carpal tunnel syndrome, and the amyloidosis associated with endocrine tumors such as medullary carcinoma of the thyroid, and the alpha-synuclein associated disease is selected from Parkinson's disease and Lewy body disease.

46. (New) The pharmacological agent of claim 45 wherein said amyloid disease for treatment is Alzheimer's disease.

47. (New) The pharmacological agent of claim 43 wherein the therapeutically effective amount of the material has an amyloid inhibitory activity or efficacy greater than 50%.

48. (New) The pharmacological agent of claim 45 wherein the disease related to alpha-synuclein is Parkinson's disease.

49. (New) A method for isolating amyloid inhibitory components from *Uncaria tomentosa* plant matter, the method comprising the steps:

a) preparing a methanol extract of the plant matter;

b) running the extract through an LH-20 first column or the like that comprises hydroxy group containing resin, or resin having hydrophobic characteristics but without any hydroxy groups, or a mixture of both;

c) eluting the first column with distilled water, followed by eluting with not more than 2-4 column bed volume washings with a dilute polar alcohol/water solution having an alcohol/water ratio not greater than 50/50, and discarding any eluate;

d) eluting the first column with one or more column bed volume washings of methanol, and collecting and drying the eluted volumes to a dried material;

e) applying an aqueous solution of the dried material to a C18 SPE second column or the like that comprises a hydrophobic resin, the second column having been preparatorily equilibrated in a solvent A comprising about 95% water/5% acetonitrile, and then eluting the second column with more solvent A and discarding the eluate;

f) eluting the second column with a mixture of solvent A containing 10-15% of a solvent B comprising about 95% acetonitrile/5% water and collecting and drying the eluted volumes to a dried material;

g) making one or more injections of a solution of the dried material in a solvent selected from the group of solvents consisting of water, water/dilute alcohol and solvent comprising solvent A and no more than 10% solvent B, into an HPLC instrument having a diode array uv/vis detector with a graphic display, the HPLC instrument further comprising a reverse-phase column;

h) eluting the material through the HPLC column using a solvent gradient profile as follows: 10% solvent B for about the first 20 minutes from start of elution, 10 to 100% solvent B gradient for about minutes 20 to 30 from start of elution, and 100 to 10% solvent

B gradient for about minutes 30 to 32 from start of elution, while observing graphic display peaks over time on the uv/vis detector during the elution gradient; and

i) separating the eluate and collecting at least one fraction component at a selected elution time, the fraction selected from the group of fraction components defined with elution times as fraction G (~13-14 minutes), fraction F (~15-16 minutes), fraction H (~17-20 minutes), fraction I (~21 minutes), fraction J (~22 - 23 minutes), fraction K1 (~24 minutes), fraction K2 (~25 minutes), fraction L (~26-27 minutes), fraction M (~27-28 minutes), and fraction N (~28-29 minutes), the elution times corresponding to times associated with the graphic display peaks.

50. (New) The method of Claim 49 wherein the elution of step f is an elution with sovent A containing about 12.5% solvent B, and at least one of the fractions collected in step i is fraction H (~17-20 minutes).

51. (New) A pharmaceutical agent comprising a therapeutically effective amount of a material made according to the process of claims 49, the therapeutic amount of the material selected for efficacy in treating an amyloid disease or a disease related to alpha-synuclein in a patient.